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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/538,396	03/29/2000	Pramod B. Mahajan	1116	6440

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EXAMINER
IBRAHIM, MEDINA AHMED

ART UNIT	PAPER NUMBER
1638	19

DATE MAILED: 01/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/538,396	MAHAJAN ET AL.	
	Examiner	Art Unit	
	Medina A Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *2-8,12 and 14-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *2-8,12 and 14-18, 20-21 and 23-39* is/are rejected.

7)☐ Claim(s) *19 and 22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/18/02 has been entered.

2. Amendment D has been entered. Claim 13 has been cancelled. Claims 16-39 have been added. Therefore, claims 2-8, 12 and 14-39 are pending and are under examination.

New Matter

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 24 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite a "non-human host cell". However, the word "non-human" has no basis in the specification or in the claims as originally filed, and is considered to be a new matter.

Applicant is required to delete the "non-human", since it has no basis in the specification or in the claims as originally filed.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2-8, 12 and 14-39 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible utility or a well-established utility.

The claims are drawn to the isolated polynucleotide of SEQ ID NO: 1 encoding SEQ ID NO: 2, a polynucleotide having at least 80%, 85%, 90% or 95% sequence identity to SEQ ID NO: 1 and encoding a polypeptide having ATP-dependent DNA binding activity and transgenic plant/plant/seed comprising said polynucleotide. The claims are also drawn to a polynucleotide that hybridizes to SEQ ID NO: 1 under specified hybridization conditions and encoding a polypeptide having ATP-dependent DNA binding activity, transgenic plant, plant cell and seeds comprising said polynucleotide, a polynucleotide encoding a polypeptide comprising at least 20 contiguous amino acids of SEQ ID NO: 2, and a polynucleotide of at least 30 contiguous bases of SEQ ID NO: 1.

Applicant asserts that the polynucleotide sequence of SEQ ID NO: 1 encoding SEQ ID NO: 2 has the utility of encoding a polypeptide having ATP-dependent DNA binding activity. However, based upon Applicant's disclosure, the claims do not meet the utility requirements under the current utility guidelines for the following reasons: 1) the predicted function is based solely upon sequence comparison with a Rad50 gene of

yeast from the prior art (see page 2 and Examples 1-2). 2) no specific use of a polypeptide having ATP-dependent DNA binding activity or Rad50 activity in a plant has been disclosed. 3) the biological functions of Rad50 gene in plants have not been documented. 4) ATP-dependent DNA binding and Rad50 activity are not specific functions.

The specification, page 2, states that yeast Rad50 gene encodes a protein that contains an ATP-binding site and plays crucial role in meiotic recombination and DNA repair during vegetative growth. The specification also discloses domains that SEQ ID NO: 2 shares with the prior art *Rad50* proteins (page 62, Example 4 of the specification). However, the state of the art teaches that sequence homology alone is insufficient to determine the functional activity of a gene/protein. For example, an article from Science Journal (vol. 292, pp. 1486-1487, 2001(X)) reveals plant and animal genes that share an overall secondary structure and six domains of functional importance, which are still sufficiently divergent in that their function cannot be determined by sequence similarity alone. Bork et al (Genome Research, Vol. 10, 2000, pp. 398-400 (Y)) also cautions using sequence comparison to predict protein function because of known error margins for high throughput computational methods (see page 398, columns 1-3; page 399, col.3 and paragraph bridging columns 2 and 3). Therefore, sequence homology alone cannot be used to determine protein function.

While Applicants are not required to provide empirical data to verify Rad50 activity by Applicants' SEQ ID NO: 2, a functional assignment based upon sequence alignments should be a starting point for determining a particular activity of a protein

and should not replace empirical verification of a tentative functional assignment. It is apparent that further research not considered to be routine would be required before one skilled in the art would know how to use Applicants' SEQ ID NO: 1 encoding SEQ ID NO: 2 to achieve a desired trait in a plant. Therefore, the immediate use of Applicants' SEQ ID NO: 1 encoding SEQ ID NO: 2 is unclear. It has been established in the courts that a utility which requires or constitutes carrying further research to identify or reasonably confirm a "real world' context of use is not a substantial utility.

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point---where specific benefits exist in currently available from---there is insufficient justification for permitting an applicant to engross what may prove to be a broad field"

While a protein having DNA repair activity would have substantial utility to the public, Applicants' claimed invention is not refined and developed to the point where it would have an immediate benefit to the public. Therefore, one skilled in the art cannot readily take Applicant's claimed invention and achieve the asserted utility, based upon Applicant's disclosure. In addition, Applicants' specification is silent as to the specific function of a protein having ATP-dependent binding activity in a plant.

Regarding the claims drawn to a polynucleotide having at least 80%, 85%, 90% or 95% sequence identity to SEQ ID NO: 1, a polynucleotide that hybridizes thereof under specified hybridization conditions and encoding a polypeptide having ATP-dependent DNA binding activity, transgenic plant, plant cell and seeds comprising said polynucleotide, a polynucleotide encoding a polypeptide comprising at least 20 contiguous amino acids of SEQ ID NO: 2, and a polynucleotide of at least 30 contiguous

of SEQ ID NO:1, since SEQ ID NO:1 encoding SEQ ID NO:2 does not have utility as discussed above, sequences less than 100% sequence identity therefore would not have utility.

Furthermore, there is no well-established utility for the claimed SEQ ID NO: 1-2, since there is no utility for probes, primers or antibodies to the expressed gene product of a gene having no known function. Therefore, in view of the reasons set forth above, the claimed sequences do not have a real-world use and, therefore, the claimed invention lacks utility.

Claim Rejections - 35 USC § 112

Claims 2-8, 12 and 14-39 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Assuming SEQ ID NO: 1 encoding SEQ ID NO: 2 has ATP-dependent DNA binding activity and can be used to "modulate the efficiency with which heterologous nucleic acids are incorporated into the genomes of a target plant cell" and create novel recombinantly engineered crops such as maize (page 2, 2nd full paragraph), it is unclear from Applicant's disclosure how Rad50 or a polypeptide having ATP-dependent DNA binding activity is involved in DNA repair (homologous or non-homologous) and how Applicants' SEQ ID NO:1 can be used to achieve "efficiency with which heterologous nucleic acids are incorporated into the genomes of a target plant cell"

In the event that Applicant provides evidence that SEQ ID NO: 1 encoding SEQ ID NO: 2 has specific DNA repair activity and can be used to "modulate the efficiency with which heterologous nucleic acids are incorporated into the genomes of a target plant cell", the enablement rejection to claims broadly drawn to an isolated polynucleotide having at least 80%, 85%, 90% or 95% sequence identity to SEQ ID NO: 1, a polynucleotide that hybridizes thereof under specified hybridization conditions and encoding a polypeptide having ATP-dependent DNA binding activity, transgenic plant, plant cell and seeds comprising said polynucleotide, a polynucleotide encoding a polypeptide comprising at least 20 contiguous amino acids of SEQ ID NO:2, and a polynucleotide of at least 30 contiguous of SEQ ID NO:1polynucleotide will be maintained because Applicant has not provided guidance for how to obtain and use the polynucleotides.

3. Applicant has not provided sufficient guidance as how to obtain any and all polynucleotides having the claimed structural property and still encoding a polypeptide having the desired functional activity. No guidance has been provided for any modification to SEQ ID NO: 1 that resulted the polynucleotides of claims 12, 14, 16-17, 20-21 and 39. Applicant has not provided guidance regarding which region in SEQ ID NO: 1 will tolerate such modifications. The specification is not enabling for a polynucleotide encoding any 20 contiguous amino acids of SEQ ID NO: 2 or a polynucleotide comprising any 30 contiguous bases of SEQ ID NO: 1 that retains ATP-dependent DNA binding activity. While the specification provides general guidance about determination of sequence identity and assays of testing protein activity, specific

guidance are required for modifications to SEQ ID NO: 1 so that a polynucleotides having both the desired structural and functional characteristics can be obtained.

The state of the prior art teaches that structural identity between two DNA/protein sequences does not necessarily mean that the sequences will have the same function, even if the percent sequence identity is relatively high. For example, Lazar et al (Molecular and Cellular Biology, March 1988, Vol. 8, No. 3, pp. 1247-1257 (U)) teach that a mutation of aspartic acid 47 and leucine 48 of transforming growth factor alpha results in different biological activities (see at least the Title). Broun et al (Science, 13 November 1998, vol. 282, pp. 131-133 (U)) teach that as few as four amino acid substitutions in a protein can change the protein activity (Abstract). Examiner notes that the nucleic acid sequences encoding the proteins disclosed by either Lazar or Broun would share at least 90% or 95% sequence identity and would hybridize to each other under the defined stringency conditions. Therefore, it is unpredictable whether modifications to DNA/protein will retain the desired functional activity and that sequence identity alone cannot be used to predictably determine the function of a protein/DNA.

In addition, no transgenic plant with a desired phenotype as result of expressing exemplified or nonexemplified sequences have been disclosed.

Therefore, given the lack of guidance as discussed supra, the unpredictability; lack of working examples, the state of the art, one skilled would not be able to practice the invention as broadly claimed.

See *Amgen Inc. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1027 (Fed. Cir. 1991) where the court held that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Written Description

Claims 2-8, 12 and 14-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to an polynucleotide of SEQ ID NO: 1 encoding SEQ ID NO: 2, a polynucleotide having at least 80%, 85%, 90% or 95% sequence identity to SEQ ID NO: 1 and encoding a polypeptide having ATP-dependent DNA binding activity and transgenic plant/plant/seed comprising said polynucleotide. The claims are also drawn to a polynucleotide that hybridizes to SEQ ID NO: 1 under specified hybridization conditions and encoding a polypeptide having ATP-dependent DNA binding activity, transgenic plant, plant cell and seeds comprising said polynucleotide, a polynucleotide encoding a polypeptide comprising at least 20 contiguous amino acids of SEQ ID NO: 2, and a polynucleotide of at least 30 contiguous bases of SEQ ID NO: 1.

The claimed invention does not meet the current written description requirements for the following reasons. Firstly, ATP-dependent DNA binding activity is not a specific function. Secondly, the specification only describes SEQ ID NO: 1 encoding SEQ ID NO: 2. Thirdly, substantial variation in structures and function are expected among

polynucleotides that share 30 contiguous bases and polynucleotides encoding polypeptides comprising 20 contiguous amino acids of SEQ ID NO: 2. Therefore, disclosure of SEQ ID NO: 1 does not provide adequate written description for all polynucleotides having at least 80%, 85%, 90% or 95% sequence identity to SEQ ID NO: 1, all polynucleotides that hybridize to SEQ ID NO: 1 under the specified hybridization conditions, all polynucleotides encoding a polypeptide comprising at least 20 contiguous amino acids of SEQ ID NO: 2, and all polynucleotide comprising at least 30 contiguous bases of SEQ ID NO: 1. Since Applicant has not described a single species of the polynucleotides of claims 12, 14, 16-17, 20-21 and 39, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that one skilled in the art would recognize that Applicants are in possession of the invention as broadly claimed. In addition, since Applicants has not described the polynucleotides as discussed above, recombinant expression cassettes, transgenic plant/plant cell/seeds of claims 2-8, 23-38 have similarly not been described. See Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices). See, also *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was atented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 39 is rejected under 35 U.S.C. 102(b) as being anticipated by Dolganov (see attached Sequence Search Result, pages 1-2)

The claim is directed to an isolated polynucleotide comprising a nucleic acid sequence which encodes at least 20 contiguous amino acids of SEQ ID NO: 2.

Dolganov teaches an isolated nucleic acid sequence encoding a polypeptide having at least 31 contiguous amino acids of SEQ ID NO: 2 (see attached Sequence search Results, pages 1-2). Therefore, the claimed invention is anticipated by the reference.

Remarks

A nucleic acid sequence of SEQ ID NO: 1 and nucleic acid sequences encoding SEQ ID NO: 2 are free of the prior art of record.

No claim is allowed.

Papers related to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmission 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Medina A. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday-Thursday from 8:30AM to 5:30PM and every other Friday 9:00AM to 5:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

12/31/02
Mai

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